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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,620	12/04/2001	Ana M. Rodriguez	GC647-2	3754

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EXAMINER

EPPERSON, JON D

ART UNIT

PAPER NUMBER

1639

DATE MAILED: 09/04/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary <i>Pfc Cuy</i>	Application No.	Applicant(s)
	10/008,620	RODRIGUEZ ET AL.
	Examiner	Art Unit
	Jon D Epperson	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 16 July 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-6 and 8-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-6 and 8-16 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>10,13</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on July 16, 2003 (Paper No. 16).

Priority Claims

2. The priority filing date of December 4, 2000 is acknowledged for CIP 09/729,520.

Status of the Claims

3. Claims 1-17 were pending in the application. In response to the Restriction Requirement, applicants cancelled claim 7 and 17 i.e., Group II (see Paper No. 16). Therefore, claims 1-6 and 8-16 are pending and examined on the merits (see below i.e., Response to Restriction and/or Election of Species).

Response to Restriction and/or Election of Species

4. Applicant's election of Group I (i.e., claims 1-6 and 8-16) in Paper No. 16 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Applicant's election of species in Paper No. 16 is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a)).

6. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

7. The information disclosure statements (i.e., Paper Nos. 10 and 13), fail, in part, to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because two publications cited therein, Quikchange and Tu et al, PCT search report, lack publication dates, a necessary element for consideration. While the other patent and other publications cited therein, and supplied, therewith, have been considered as to the merits, these two publications have not. Applicant is advised that the date of any re-submission of these citations contained in this information disclosure statement or the submission of the missing element – their publication dates – will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 C(1).

Specification

8. The specification is objected to because of the following informalities:

A. The “Bauer” reference(s) in the specification have the wrong Patent Nos. (e.g., see specification, page 2, line 27 wherein the Patent No. should read “5,932,419” not “5,923,419.” Appropriate correction is required.

9. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant’s cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. **Claims 1-2** recite the limitations “the nucleotides” and “said nucleotides” (e.g., see claim 1, step 1(d)). There is insufficient antecedent basis for this limitation in the claim. Therefore, claims 1, 2 and all dependent claims are rejected under 35 USC 112, second paragraph.

B. **Claims 1,4** recite the limitation “the mixture” (e.g., see claim 1, step 1(e)). There is insufficient antecedent basis for this limitation in the claim. Therefore, claims 1, 4 and all dependent claims are rejected under 35 USC 112, second paragraph.

C. For **claim 3**, the term “saturation concentration” is vague and indefinite.

Applicants define “saturation concentration” in the specification as “the mutagenic and corresponding non-mutagenic primers will be added in limiting quantities as compared to other reaction starting products.” However, the Examiner contends that this definition is inadequate because it is not clear what is meant by “limiting quantities” and it is also not clear which “starting products” are to be used as the basis of reference. Applicants are requested to clarify and/or correct. Therefore, claim 3 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

D. **Claim 6** recites the limitation “said protein product” (e.g., see claim 6, line 1).

There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 6 and all dependent claims are rejected under 35 USC 112, second paragraph.

E. **Claims 8, 10-12** recite the limitation “the primers” and/or “said primers” (e.g., see claim 8, step 1(c)). There is insufficient antecedent basis for this limitation in the claim.

Therefore, claims 8, 10-12 and all dependent claims are rejected under 35 USC 112, second paragraph.

F. **Claims 8** recite the limitation “the mixture” (e.g., see claim 8, step 1(e)). There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 8 and all dependent claims are rejected under 35 USC 112, second paragraph.

G. **Claim 9** recites the broad recitation 3 to 15, and the claim also recites 4 to 7, which is the narrower statement of the range/limitation. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set

forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). Therefore, claim 9 and all dependent claims are rejected under 35 USC 112, second paragraph.

H. **Claims 13-14** recite the limitation "at least one mutagenic primer" (e.g., see claim 13, line 1). There is insufficient antecedent basis for this limitation in the claim. Therefore, claims 13-14 and all dependent claims are rejected under 35 USC 112, second paragraph.

I. **Claim 16** recites the limitation "said protein product" (e.g., see claim 16, line 1). There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 16 and all dependent claims are rejected under 35 USC 112, second paragraph.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6, 8 and 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Bauer et al (US Patent No. 5,932,419) (Date of Patent is August 3, 1999) (IDS Paper #10).

For *claims 1, 8 and 12*, Bauer et al discloses a method for introducing site-directed mutations into circular DNA molecules of interest by means of mutagenic primer pairs (see Bauer et al, entire document, especially abstract), which anticipates claim 1.

For example, Bauer et al discloses using a double stranded circular DNA “template” (see Bauer et al, column 2 lines 42-45; see also column 5, lines 56-57; see also column 6, line 36 showing that single stranded DNA may also be used as templates), which anticipates “obtaining a template nucleic acid” in claims 1(a). Furthermore, Bauer et al discloses the use of mutagenic primer “pairs” that contain at least one mutation site with respect to the target sequence (see Bauer et al, abstract; see also column 2, lines 44-46; see also column 4 lines 37-47; see also column 6, last paragraph), which anticipates claim 1 (b) and (c).

Bauer et al discloses hybridizing said “mutagenic” primer pairs to the target sequence (see Bauer et al, column 2, lines 51-52), which anticipates claim 1 (d). Furthermore, Bauer et al discloses the production of more than one mutant strand (i.e., a library of mutant template nucleic acids) via linear cyclic amplification reactions (see Bauer et al, column 2, last paragraph; see especially line 56 and lines 61-62; see also column 7, last paragraph and column 8), which anticipates claim 1 (e).

In addition, Bauer et al discloses that the primers can be in “opposite orientation” (see Bauer et al, figure 1B wherein arrows show an “opposite orientation”; see also column 4, line 13; see also column 5, line 53).

For *claim 2*, Bauer et al discloses the use of mutagenic primer pairs that are annealed to “opposite” strands of a circular DNA double stranded template i.e., they are separate primers (see Bauer et al, column 2, lines 51-52).

For *claims 3,11*, Bauer et al discloses first and second oligonucleotides at a concentration of 100 ng/ul (see Bauer et al, column 12, lines 47 and 49), which anticipates claim 3 because 100 ng/ul is less than saturation concentration.

For *claim 4*, Bauer et al discloses that the transformants may contain non-mutagenized parent strands that are eventually digested AFTER several cycles of linear cyclic amplification (see Bauer et al, column 9, paragraph 1).

For *claims 5-6 and 15-16*, Bauer et al discloses a template strand that corresponds to the lacZ protein product i.e., β-galactosidase enzyme (see Bauer et al, column 12, “EXAMPLES”).

For *claims 13-14*, Bauer et al discloses “substitutions, insertions and deletions” that are “well known” to persons of skill in the art wherein the mutagenic primers contain “one or more mutagenic sites” (see Bauer et al, column 7, paragraph 1; see also column 6, line 57-58).

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12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-6, 8 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer et al (US Patent No. 5,932,419) (Date of Patent is **August 3, 1999**) and Stemmer et al (US Patent No. 5,512,463) (Date of Patent is **April 30, 1996**) (IDS Paper # 10).

For **claims 1-6, 8 and 11-16**, Bauer et al teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates claims 1-6, 8 and 11-16 and, consequently, also renders obvious claims 1-6, 8 and 11-16.

The prior art teaching of Bauer et al differs from the claimed invention as follows:

For *claim 9*, the prior art teaching of Bauer et al is deficient in that it does not teach the use of 3 to 15 primers.

For *claim 10*, the prior art teaching of Bauer et al differs from the claimed invention by not specifically reciting the use of “discontiguous” primers. Bauer et al only teaches the use of “overlapping” or “partially overlapping” primers (e.g., see Bauer et al, column 7, lines 10-12).

However, Stemmer et al teaches the following limitations that are deficient in Bauer et al:

For *claims 1-6, 8 and 11-16*, Stemmer et al (see entire document) also discloses methods for producing a library of nucleic acids by preparing a first and second primer population that hybridizes to a double-stranded nucleic acid template and is subsequently amplified (see Bauer et al, especially paragraph bridging columns 17-18; see also figure 6B wherein the “X” designations in the shaded region represent a library of primers with variable substitutions at each of the “X” positions), which reads on claims 1-6, 8 and 11-16. However, Stemmer et al does not teach “linear” amplification (Bauer et al teaches linear amplification, see above), Stemmer only teaches “exponential” amplification i.e., PCR.

For *claim 9*, Stemmer et al discloses a specific example of four primers wherein position 6 contains G and A and the complementary primer contains C and T producing a total of four primers. Stemmer et al also provides a general teaching that would allow a person of skill in the art to immediately envision any number of primers (e.g., see Stemmer et al, column 18, paragraph 1).

For *claim 10*, Stemmer et al (see entire document) teaches that the primers are discontiguous (see Stemmer et al, column 17, lines 30-31 “The primers may be ... non-overlapping”).

It would have been obvious to one skilled in the art at the time the invention was made to replace the “exponential” amplification (i.e., PCR) method as taught by Stemmer et al for making combinatorial nucleic acid libraries with the “linear” amplification as taught by Bauer et al because Bauer et al explicitly states that “linear” amplification is better than “exponential” amplification because it does not require a “ligation” step which would “reduce the time and expense required to carry out ... conventional methods of site directed mutagenesis” (see Bauer et al, column 11, lines 36-40). Consequently, one of ordinary skill in the art would have been motivated to use the “linear” amplification as taught by Bauer et al “to reduce the time and expense” for generating libraries and transforming host cells as mentioned above. Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Stemmer et al teaches that both “overlapping” and “nonoverlapping” primers can be used to generate the nucleic acid libraries which would encompass the “overlapping” primers or “partially overlapping” primers disclosed by Bauer et al (see Bauer et al, column 7, lines 10-12).

Double Patenting

Claim Rejections – 35 USC § 101

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15. A rejection based on double patenting of the “same invention” type finds its support in the language of 35 USC 101 which states that “whoever invents or discovers any new and useful process ... may obtain a patent therefore ...” (Emphasis added). Thus, the term “same invention,” in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

16. Claims 1-6 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-6 of copending Application No. 20020155439 A1 (Serial No. 09/729,520). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Non-Statutory Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-6 and 8-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent Application No. 20020155439 A1 (referred to as ‘439) in view of Bauer et al (US Patent No.

5,932,419) (Date of Patent is **August 3, 1999**) and Stemmer et al (US Patent No. 5,512,463)

(Date of Patent is **April 30, 1996**).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examiner application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986).

Here, claims 1-6 of ‘439 recite the exact same method as those claimed by Applicant in claims 1-6 of the present application (see Statutory Double Patenting rejection above). The method of claims 1-6 in ‘439 fail to disclose primers between 3 to 15 primers or “discontiguous” primers. However, the combined teachings of Bauer et al and Stemmer et al teach between 3 to 15 primers and “discontiguous primers” and all other limitations for claims 1-6 and 8-16 (see 35 U.S.C. § 103(a) rejection above, which is incorporated in its entirety herein by reference). It would have been obvious to modify the method of claims 1-6 of ‘439 to use the “discontiguous” primers and a library of primers containing between 3 to 15 primers as taught by the combined teachings of Bauer et al and Stemmer et al because the combined teachings of Bauer et al and Stemmer et al falls within the scope of the claims 1-6 of ‘439 (i.e., the references represent analogous art) and the combined teachings of Bauer et al and Stemmer et al explicitly state that their exemplified embodiments will “reduce the time and expense” (see Bauer et al, column 7, lines 10-12).

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217.. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
August 28, 2003

BENNETT CELSA
PRIMARY EXAMINER

